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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,309	01/03/2001	Christine Andreoni	PF82PCTSEQ/d	7033

25666 7590 10/01/2004

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EXAMINER	
SHAHNAN SHAH, KHATOL S	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/647,309	ANDREONI ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 30 July 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): 112 second rejection..

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *NONE*.

   Claim(s) objected to: *NONE*.

   Claim(s) rejected: *22-24 and 26-39*.

   Claim(s) withdrawn from consideration: *40*.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☒ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). *7/30/04*.

10. ☐ Other: _____

Attachment to Advisory Action

1. Applicants' reply to a final office action under 37 CFR 1.116, received 7/30/04 is acknowledged.

2. Claims 22-24 and 26-40 are pending in the application.

3. Claims 22-24 and 26-39 are under consideration. Claim 40 is withdrawn from consideration as being drawn to non-elected inventions.

Petition for Withdrawal of Finality

4. Applicants' request to petition under 37 CFR 1.181 filed 7/30/2004 is DISMISSED because a proper petition required under 37 CFR 1. 181 has not been submitted to this office. Applicants arguments in the response submitted 7/30/2004 has been noted. Applicants argue that applicants' amendments did not constitute a basis for the new grounds of rejection under 35 U.S.C. 103 (a) has been noted. It is the examiner's position the applicants' amendments did constitute basis for the new grounds of rejection under 35 U.S.C. 103 (a) because the amended claims recite a method of improving immunity upon intranasal administration of the claimed compound. Original claims were drawn to intended use of the claimed compound. Therefore, applicants' amendments necessitated the new ground(s) of rejection in the office action.

Information Disclosure Statement

5. Applicants' Information Disclosure Statement, received 7/30/04 is acknowledged. The references have been considered by the examiner. See attached 1449.

Rejections Withdrawn

6. Rejection of claim 22 under 35 USC § 112 second paragraph made in paragraph 14 of the office action mailed 4/05/2004 is withdrawn in view of applicants' amendment.

Rejections Maintained

7. Rejection of claims 22-24 under 35 USC § 103(a) made in paragraph 16 of the office action mailed 4/05/2004 is maintained.

The rejection was as stated below:

Claims 22-24 and 26- 39 are rejected under 35 U.S.C. 103(a) as being obvious over Rauly et al. (Research in Immunology, Vol. 149, No.1, pp. 99, January 1998) in view of Cooper et al. (Journal of infectious, Vol. 147, No.2, pp. 312-317, February 1983).

Claims are drawn to a method of improving immunity in a mammal through administration of a pharmaceutical composition comprising *Klebsiella pneumoniae* outer membrane protein.

Rauly et al. teach a method of using an outer membrane protein (OmpA) of *Klebsiella pneumoniae* for enhancing or improving immunity of a mammal with respect to an antigen (see page 99). Rauly et al. teach a protein obtained by recombinant process. Rauly et al. teach use of the G1 antigen of RSV coupled to rP40 protein of *Klebsiella pneumoniae* the same conjugate as the claimed invention. Rauly et al. teach that the conjugate generated strong antibody response even in the absence of any adjuvant. Rauly et al. do not teach intranasal administration. However Cooper et al. teach intranasal administration of *Klebsiella pneumoniae* antigens in mice (see abstract). It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the methods of Rauly et al. and Cooper et al. to obtain the claimed invention. One of ordinary skill in the art would have been motivated to administer the pharmaceutical composition of Rauly et al. intranasaly by the teachings of Cooper et al. that protection from disease also follows after intranasal immunization of

Klebsiella pneumoniae and antibodies develop in the serum after intranasal immunization (i.e improving immunity).

Applicants' arguments filed 7/30/2004 have been fully considered but they are not persuasive.

Applicants argue that the office no motivation to combine the references is improper. Applicants further argue that Cooper et al. teaches away from the claimed method of improving immunity because intranasal administration of inactivated *Klebsiella pneumonaie* bacteria generated low levels of antibody.

In response to applicants' argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, One of ordinary skill in the art would have been motivated to administer the pharmaceutical composition of Rauly et al. intranasaly by the teachings of Cooper et al. that protection from disease also follows after intranasal immunization of *Klebsiella pneumoniae* and antibodies develop in the serum after intranasal immunization. Using Rauly'protein obtained by recombinant process intranasaly as taught by Cooper et al. would have improved immunity.

8. Rejection of claims 22-24 under 35 USC § 103(a) made in paragraph 17 of the office action mailed 4/05/2004 is maintained.

The rejection was as stated below:

Claims 22-24 and 26- 39 are rejected under 35 U.S.C. 103(a) as being obvious over Haeuw et al. (European Journal of Biochemistry, Vol. 255, pp. 446-454, 1998) in view of Cooper et al. (Journal of infectious, Vol. 147, No.2, pp. 312-317, February 1983).

Claims are drawn to a method of improving immunity in a mammal through administration of a pharmaceutical composition *Klebsiella pneumoniae* outer membrane protein.

Haeuw et al. teach using an outer membrane protein (OmpA) of *Klebsiella pneumoniae* for enhancing or improving immunity of a mammal with respect to an antigen (see abstract). Haeuw et al. teach a protein obtained by recombinant process (see cloning and expression page 447). Haeuw et al. teach detergent Zwittergent 3-14 (see reagents page 447). Haeuw et al. teach use of the G1 antigen of RSV coupled to rP40 protein of *Klebsiella pneumoniae* the same conjugate as the claimed invention (page 447). Haeuw et al. teach that the conjugate generated strong antibody response even in the absence of any adjuvant (see pages 448 and 451). Haeuw et al. do not teach intranasal administration. However Cooper et al. teach intranasal administration of *Klebsiella pneumoniae* antigens in mice (see abstract). It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the methods of Rauly et al. and Cooper et al. to obtain the claimed invention. One of ordinary skill in the art would have been motivated to administer the pharmaceutical composition of Haeuw et al. intranasaly by the teachings of Cooper et al. that protection from disease also follows after intranasal immunization of *Klebsiella pneumoniae* and antibodies develop in the serum after intranasal immunization (i.e improving immunity).

Applicants' arguments filed 7/30/2004 have been fully considered but they are not persuasive.

Applicants argue that the office no motivation to combine the references is improper. Applicants further argue that Cooper et al. teaches away from the claimed method of improving immunity because intranasal administration of inactivated *Klebsiella pneumonaie* bacteria generated low levels of antibody.

In response to applicants' argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, One of ordinary skill in the art would have been motivated to administer the pharmaceutical composition of Haeuw et al. intranasaly by the teachings of Cooper et al. that protection from disease also follows after intranasal immunization of *Klebsiella pneumoniae* and antibodies develop in the serum after intranasal immunization. Using Haeuw'protein obtained by recombinant process intranasaly as taught by Cooper et al. would have improved immunity.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol S Shahnan-Shah whose telephone number is (571)-272-0863. The examiner can normally be reached on 7:30am-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith can be reached on (571)-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

September 27, 2004

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER